Complete Summary

GUIDELINE TITLE

Antiretroviral therapy.

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2008 Jan. 115 p. [18 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2007 Aug. 50 p. [18 references]

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- July 24, 2008, Ziagen (abacavir sulfate): The U.S. Food and Drug Administration (FDA) has notified the maker of abacavir and abacavir-containing medications of the need to add information to the current BOXED WARNING about the recommendation to test all patients for the HLA-B*5701 allele before starting or restarting therapy with abacavir or abacavir-containing medications.
- March 12, 2008, Prezista (darunavir): The U.S. Food and Drug Administration (FDA) and Tibotec Therapeutics notified healthcare professionals of changes to the WARNINGS section of the prescribing information for Prezista (darunavir) tablets regarding the risk of hepatotoxicity, specifically, drug induced hepatitis in patients receiving combination therapy with Prezista/ritonavir.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Human immunodeficiency virus (HIV) infection
- Acquired immunodeficiency syndrome (AIDS)
- Adverse effects of antiretroviral therapy, including:
    - Bone marrow suppression
    - Pancreatitis
    - Lactic acidosis/hepatic steatosis
    - Hepatotoxicity
    - Renal toxicity
    - Myopathy/myositis

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Hematology
Infectious Diseases
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Pharmacists
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To provide guidelines for antiretroviral treatment of human immunodeficiency virus (HIV) infection

TARGET POPULATION

Human immunodeficiency virus (HIV)-infected patients

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation/Diagnosis

1. Viral load (plasma viral load)
2. Lymphocyte subsets (CD4 cell counts)
3. Human immunodeficiency virus (HIV) resistance assays
4. Antiretroviral serum levels (therapeutic drug monitoring) (not recommended)
5. Laboratory monitoring of antiretroviral therapy side effects
6. Monitoring for allergic reactions

Treatment/Management

1. Patient involvement in treatment initiation and planning, including:
    - Patient education and counseling on risks and benefits of therapy, measures to reduce HIV transmission, medication schedules, strict adherence, and side effects of therapy
    - Assessment of patient commitment to adherence to therapy
2. Selecting an initial antiretroviral regimen
    - For anti-retroviral (ARV)-naïve patients, combination of two nucleoside reverse transcriptase inhibitors (NRTIs) plus either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor (NNRTI)
    - For patients previously treated with only nucleoside analogs, observation and reevaluation of treatment guided by HIV resistance studies
3. Assessment and insurance of patient adherence to therapy
4. Changing a successful highly active antiretroviral therapy (HAART) regimen
    - Review of previous resistance testing
5. Second-line regimens and salvage HAART
    - Consultation with HIV Specialist
    - Using a drug from a class not used in the first-line regimen, using agents in novel antiretroviral (ARV) classes or with unique resistance profiles
6. Treatment for acute HIV infection
    - Laboratory testing including:
        - Plasma HIV ribonucleic acid (RNA) assay in conjunction with HIV-1 antibody test
        - Confirmatory HIV antibody testing
    - Patient education and counseling
7. Management of treatment interruption
    - Patient education about increased risk of transmitting HIV
    - Changing regimen before discontinuation
    - Continuing treatment for co-infections
8. Patient referral to research studies

MAJOR OUTCOMES CONSIDERED

- Effectiveness of antiretroviral therapy in suppressing human immunodeficiency virus (HIV) replications, restoring and/or preserving immune function, reducing HIV-related morbidity and mortality, and improving quality of life
- Adverse effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trials
II. Evidence from one or more well-designed clinical trials without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with human immunodeficiency virus (HIV) infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

* Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Committee
- Women's Health Committee
- Substance Use Committee
- Physician's Prevention Advisory Committee
- Pharmacy Committee

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the quality of the evidence (I, II, III) are provided at the end of the "Major Recommendations."

Goals, Benefits, and Risks of Highly Active Antiretroviral Therapy (HAART)

Clinicians should prescribe a HAART regimen that is best able to delay disease progression, prolong survival, and maintain quality of life through maximal viral suppression (see Table below). **(I)**

Table: Goals of Antiretroviral Therapy
• Maximal and durable suppression of viral replication (measured by viral load assays) • Restoration and/or preservation of immune function • Reduced human immunodeficiency virus (HIV)-related morbidity and mortality • Improved quality of life • Limitation of the likelihood of viral resistance to preserve future treatment options

The clinician should involve the patient in the decision-making process when determining whether to implement antiretroviral (ARV) therapy. The clinician should review the benefits and risks of treatment for each individual patient. **(III)** (See Table 2 in the original guideline document.)

Deciding Whether to Initiate ARV Therapy

Initiation of HAART is recommended for patients who:

- Are symptomatic from HIV **(I)**, *or*
- Have an acquired immunodeficiency syndrome (AIDS)-defining condition, including those with CD4 counts <200 mm^3 **(I)**, *or*
- Are asymptomatic with two successive measurements of CD4 counts <350 cells/mm^3 **(I)**
  and
- Patient-related barriers to adherence are minimized **(III)**

For recommendations on initiating HAART in HIV-infected pregnant women, refer to *Management of HIV-Infected Pregnant Women Including Prevention of Perinatal HIV Transmission* (see the New York State Department of Health Web site).

The decision to begin ARV therapy should be individualized and should incorporate an assessment of four major factors:

- The patient's risk of progression to illness or death if left untreated (see Appendix D in the original guideline document) **(I)**
- The patient's willingness to adhere to the therapy prescribed **(II)**
- Potential barriers to adherence **(III)**
- The risk of long-term toxicity **(III)**

Clinicians should involve patients when planning their treatment regimens. In conjunction with their clinicians, patients should make the final decision of when to initiate ARV therapy. **(III)**

Except when initiation of treatment is clinically urgent, clinicians should use more than one visit for education and counseling before committing a patient to a specific therapy. **(II)** Counseling and education should include the following:

- Available treatment options and potential benefits and risks of therapy (see Table 3 in the original guideline document)
- The need for strict adherence and the risk of viral drug resistance when adherence is suboptimal (see *The Importance of Patient Adherence* section below)
- Use of safer-sex practices and avoidance of needle-sharing activity, regardless of viral load, to prevent HIV transmission or superinfection **(II)**
- Counseling regarding specific issues relevant to the patient's individual clinical situation

Clinicians should discuss the risks and benefits of initiating ARV therapy with asymptomatic patients with two successive measurements of viral load >100,000 copies/mL and CD4 count >350 cells/mm^3. This discussion should include the increased risk of transmitting HIV in the setting of higher viral load (see Table 3 in the original guideline document).

Clinicians should follow up with patients by phone or visit within 2 weeks of initiating therapy to assess tolerance and adherence to the ARV regimen. Adherence should be reinforced at regular intervals during the course of therapy. **(III)**

Coexisting Conditions

Clinicians should strongly recommend that women presenting in the third trimester of pregnancy, and patients with acute or progressive renal insufficiency, severe thrombocytopenia, or HIV encephalopathy, initiate ARV therapy.

Clinicians should strongly recommend that patients recovering from acute opportunistic infections initiate ARV therapy as soon as it is safe based on patient tolerability and drug-drug interactions.

Table: Considerations for the Initiation of Antiretroviral Therapy in the Chronically HIV1 Infected Patient

Clinical Category	CD4 T Cell Count*	Plasma HIV RNA*	Recommendation
Symptomatic**	Any value	Any value	Treat
Asymptomatic, AIDS	CD4 T cells <350 cells/mm^3	Any value	Treat
Asymptomatic	CD4 T cells >350 cells/mm^3	>100,000 copies/mL (reverse transcriptase-polymerase chain	Some experts would recommend initiating therapy, recognizing that the

Table: Considerations for the Initiation of Antiretroviral Therapy in the Chronically HIV1 Infected Patient			
Clinical Category	**CD4 T Cell Count***	**Plasma HIV RNA***	**Recommendation**
		reaction [RT-PCR] or branched deoxyribonucleic acid [bDNA])	3-year risk of developing AIDS in untreated patients is >30%.
Asymptomatic	CD4 T cells >350 cells/mm^3	<100,000 copies/mL (RT-PCR or bDNA)	Delay therapy. Repeat laboratory assessments at least every 4 months.

* Decisions should be made after two successive measurements have been obtained.
**Signs and symptoms include but are not limited to oropharyngeal candidiasis (thrush); vulvovaginal candidiasis that is frequent or responds poorly to therapy; cervical dysplasia (moderate or severe)/cervical carcinoma *in situ*; HIV nephropathy in the setting of worsening serum creatinine; severe seborrheic dermatitis, constitutional symptoms, such as fever or diarrhea lasting >1 month; oral hairy leukoplakia; herpes zoster (shingles) involving at least two distinct episodes or more than one dermatome; thrombocytopenia; listeriosis; pelvic inflammatory disease, particularly if complicated by tubo-ovarian abscess; peripheral neuropathy; bacillary angiomatosis; or any conditions included in the CDC-defined AIDS definition.

The Importance of Patient Adherence

A team approach to achieving adherence should be used. Nurses, pharmacists, peer counselors, caseworkers, and others who work in outreach, evaluation, and support of adherence should be involved. **(III)**

The clinician should assess treatment readiness prior to initiation of treatment, adherence readiness for subsequent regimens, and adherence at every clinical visit. **(III)**

Interventions should be intensified in times of decreased adherence.

Information about patients' beliefs and attitudes should be communicated with all members of the healthcare team so that each provider can consistently address treatment adherence issues within the context of the overall treatment plan. **(II)**

If the patient is not fully committed to adhering to therapy, treatment should be delayed, and the clinician should continue to work on abating the patient's concerns. Appropriate referrals should be provided for support groups, mental health, and drug treatment. **(III)**

Refer to the original guideline document for the list of potential barriers to adherence and strategies for promoting adherence.

Selecting an Initial Antiretroviral Regimen

Clinicians should perform genotypic resistance testing before initiating treatment in ARV therapy-naïve patients to determine whether they are infected with drug-resistant virus. **(III)**

The goal of initial HAART in the ARV therapy-naïve patient should be to devise a regimen that will achieve maximal durable viral suppression (<50 copies per mL) and be tolerated for an indefinite period of time. **(I)**

Clinicians should involve their patients when deciding which HAART regimen is most likely to result in adherence. **(III)**

For ARV therapy-naïve patients, the initial HAART regimen should include a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) plus either a protease inhibitor (PI), or a non-nucleoside reverse transcriptase inhibitor (NNRTI). **(I)** When using a PI-based initial regimen, clinicians should use a ritonavir-boosted PI, unless there are relative contraindications.

Clinicians should not use nevirapine as part of the initial regimen in women with CD4 counts >250 cells/mm^3 or men with CD4 counts >400 cells/mm^3 because of an increased incidence of hepatotoxicity. **(I)**

For women considering pregnancy or likely to become pregnant, efavirenz or combination pills containing efavirenz should be avoided. If there are no alternatives for efavirenz in women of childbearing age, clinicians should strongly advise the use of effective contraception and should obtain a pregnancy test before initiating treatment. **(I)**

Selection of ARV agents should be individualized to address each patient's concurrent morbidities and medications, ability to adhere to complex regimens, and personal tolerance for adverse medication effects.

Refer to Table 6 in the original guideline document for preferred, alternative, and contraindicated combinations for initial treatment of HIV infections.

See also Appendix A of the original guideline document for specific dosing recommendations, adverse events, drug-drug interactions, and U.S. Food and Drug Administration (FDA) pregnancy categories for each ARV drug.

Monitoring of Patients Receiving ARV Therapy

Monitoring Markers of HIV Infection

Viral Load

In ARV treatment-naïve patients or patients who are on a successful regimen, plasma viral load should be measured at baseline and every 3 to 4 months thereafter. Patients with CD4 counts >500 cells/mm^3 may only require viral load monitoring every 6 months. **(III)**

Viral load should be measured immediately before initiation or change of ARV therapy and every 2 to 4 weeks after initiation or change until maximal

suppression is documented. Once maximal suppression is attained, monitoring of viral load should occur every 3 to 4 months. **(III)**

If there is a significant increase (3-fold increase or more) in viral load without clear explanation, measurement should be repeated to confirm virologic failure. **(III)**

Virologic failure should prompt the clinician to assess the patient's adherence and to check for the presence of viral resistance. **(I)**

Refer to Table 7 in the original guideline document for interpretation of viral load.

Lymphocyte Subsets

Clinicians should measure CD4 cell counts at the time of diagnosis of HIV infection and every 3 to 4 months thereafter. **(III)**

The absence of a significant CD4 cell count increase should not be interpreted as treatment failure if the viral load declines appropriately. **(III)**

HIV Resistance Assays (See Table below)

Clinicians should perform resistance testing under the following circumstances:

- At baseline in the setting of acute HIV infection, regardless of whether ARV therapy is being initiated (genotypic testing)
- In ARV therapy-naïve patients before initiation of ARV therapy (genotypic testing) **(III)**
- In patients experiencing treatment failure or incomplete viral suppression while receiving ARV therapy (genotypic and/or phenotypic testing) **(I)**

When resistance testing is indicated, it optimally should be performed while patients are either receiving therapy **(I)** or have been off therapy for less than 1 year. **(III)**

Clinicians should consult with an expert to interpret the results of resistance assays because the results of resistance assays are often complex (see the New York State Department of Health AIDS Institute Web site for Clinical Education Initiative sites available for phone consultation). **(I)**

Key Point: Resistance testing more reliably indicates drugs that are not likely to be effective rather than identifying those drugs that may suppress viral replication.

Table: Recommendations for the Use of Drug Resistance Assays*	
Clinical Setting/Recommendation	**Rationale**

Table: Recommendations for the Use of Drug Resistance Assays*	
Clinical Setting/Recommendation	**Rationale**
Prior to initiating treatment in ARV-naïve patients, including in the setting of acute HIV infection	Determine if drug-resistant virus was acquired so that an appropriate regimen may be chosen.
Virologic failure during HAART	Determine the role of resistance in drug failure, and maximize the number of active drugs in the new regimen.
Suboptimal suppression of viral load after initiation of ARV therapy (In pregnant women initiating therapy, the clinician may not have as much time to monitor for suboptimal suppression.)	Determine the role of resistance, and maximize the number of active drugs in the new regimen if indicated.
Not Generally Recommended	
More than 1 year after discontinuation of drugs	Drug-resistance mutations may become minority species in the absence of selective drug pressure and may not be detectable. Current assays may not detect minority drug-resistant species.
Plasma viral load <500 to 1,000 HIV ribonucleic acid (RNA) copies/mL (The cutoff will vary according to the manufacturer of the kit.)	Resistance assays cannot be reliably performed because of the low copy number of HIV RNA.

*Adapted from the *Department of Health and Human Services (DHHS) Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents (2006)*

Antiretroviral Serum Levels (Therapeutic Drug Monitoring)

Monitoring blood levels of ARV drugs is not currently recommended. **(III)**

Laboratory Monitoring of Antiretroviral Therapy Side Effects

Bone Marrow Suppression

Complete blood counts should be measured before initiation of ARV therapy and at least every 4 months thereafter. For patients at high risk for bone marrow toxicity (e.g., those with advanced HIV infection, those with pre-treatment cytopenias, or those who are receiving zidovudine), blood counts may have to be monitored more frequently because significant cytopenias may occur. **(III)**

Pancreatitis

When patients receiving ARV therapy present with signs and symptoms suggestive of pancreatitis, clinicians should obtain serum amylase and lipase levels. **(III)**

If signs or symptoms of pancreatitis occur in patients taking ARV medications, the clinician should temporarily suspend the entire ARV regimen. A new ARV regimen may be initiated when enzymes are normalized but should not include ARV medications that are most likely linked to pancreatitis, such as didanosine or stavudine.

An elevated serum amylase level should be confirmed with a serum lipase level. **(III)**

Clinicians should not prescribe didanosine for patients who have a history of pancreatitis. **(III)**

Lactic Acidosis/Hepatic Steatosis

When patients develop symptoms consistent with lactic acidosis syndrome in conjunction with an elevated lactate level (>2 mmol/L) and decreased serum bicarbonate (<20 mmol/L), the clinician should temporarily discontinue the entire ARV regimen while an evaluation is conducted. **(II)**

Routine monitoring of serum lactate levels is not indicated in asymptomatic patients. **(I)**

Patients who are asymptomatic and have an unexplained decrease in serum bicarbonate level (<20 mmol/L) should be promptly re-evaluated with a repeat test and a venous or arterial lactate. **(II)** If a venous lactate is mildly elevated (2.1 to 5.0 mmol/L), an arterial lactate should be obtained, and reassessment for the presence of symptoms associated with lactic acidosis should be performed. **(I)** If the lactate is persistently elevated, the arterial pH is abnormal, or the patient has become symptomatic, ARV therapy should be discontinued. **(III)**

Hepatotoxicity

Clinicians should obtain serum liver enzyme levels at baseline and every 3 to 4 months thereafter in patients receiving HAART. **(III)**

Clinicians should screen for alcohol use in patients with abnormal serum liver enzyme levels. **(III)**

<u>Use of Nevirapine</u>

Clinicians should not use nevirapine as part of the initial regimen in women with CD4 counts >250 cells/mm^3 or men with CD4 counts >400 cells/mm^3 because of an increased incidence of hepatotoxicity. **(I)**

When initiating an ARV regimen that includes nevirapine, clinicians should obtain serum liver enzymes at baseline, at the time of dose escalation (14 days), and 2 weeks after dose escalation. **(III)**

Clinicians should counsel patients to seek medical evaluation when signs and symptoms of hepatitis, severe skin reactions, or hypersensitivity reactions related to nevirapine occur. Serum liver enzymes should be obtained whenever patients develop a rash during nevirapine therapy, particularly during the first 18 weeks of therapy. **(II)**

In the setting of hepatotoxicity related to nevirapine, patients should not be rechallenged with nevirapine. **(I)**

Renal Toxicity

For all HIV-infected patients receiving ARV therapy:

Clinicians should obtain urinalysis at baseline and annually thereafter.

Clinicians should measure serum creatinine levels and calculate glomerular filtration rates at baseline and every 3 to 4 months thereafter in HIV-infected patients. **(III)**

For patients receiving tenofovir:

For patients initiating a tenofovir-containing regimen, clinicians should calculate glomerular filtration rates at baseline, 1 month, and then at least every 3 to 4 months thereafter.

Clinicians should discontinue tenofovir when patients present with symptoms suggestive of Fanconi syndrome.

For patients receiving indinavir:

Clinicians should counsel patients receiving indinavir to drink at least 48 ounces of fluid per day.

Myopathy/Myositis

Measurement of serum creatinine phosphokinase (CPK) is not routinely indicated. If the patient becomes symptomatic (e.g., muscle pain or weakness), CPK should be measured. **(II)**

Monitoring for Allergic Reactions Associated with ARV Therapy

When patients receive any new ARV drugs, clinicians should educate them about the possibility of HAART-associated allergic reactions, including a hypersensitivity reaction, and the range of possible symptoms (refer to Table 9 in the original guideline document to view ARV drugs associated with allergic reactions). **(III)**

Clinicians should discontinue offending drugs when there is a moderate to severe skin reaction, mucous membrane involvement, systemic toxicity, or fever. **(I)**

Clinicians should avoid re-challenging patients with a medication that has been associated with a hypersensitivity reaction, especially in the setting of abacavir reactions and severe NNRTI reactions. **(I)**

In patients who develop mild rash in response to nevirapine, clinicians should avoid escalating the nevirapine dose to twice daily until after the rash has resolved. For patients with moderate to severe cutaneous toxicity, nevirapine should be discontinued and should not be re-challenged. Use of an alternate NNRTI should be avoided. **(III)**

Prompt discontinuation of abacavir when a hypersensitivity reaction is suspected is necessary because symptoms will worsen over time. Once abacavir has been discontinued because of a possible or definite hypersensitivity reaction, abacavir should never be administered again. Re-challenge may result in an anaphylactic reaction with associated hypotension or death.

Changing a Successful Initial HAART Regimen

Clinicians should change a successful initial HAART regimen when the patient's adherence will be compromised by continuing the current regimen. **(III)**

When considering a change in the ARV regime due to drug toxicity, the clinician should confirm that the viral load is maximally suppressed. **(III)** If maximal viral suppression has been achieved, the clinician should substitute the offending drug. **(I)**

The clinician should review results from previous resistance testing before changing a successful regimen. **(III)**

Failure to Achieve Goals of Initial HAART

Clinicians should address adherence, obtain resistance assays, and consult with an HIV Specialist before changing HAART regimens that have failed.

Clinicians should not change an ARV regimen when there is incomplete but significant viral suppression ($\geq$0.5 log reduction, or 3-fold, from baseline viral load value) compared with baseline and a more effective HAART regimen cannot be constructed as a result of drug resistance or intolerance.

Second-Line Regimen and Salvage HAART

Clinicians should consult with an HIV Specialist when constructing a second-line regimen and salvage therapy regimens.

Clinicians should review individual ARV history and results from HIV drug resistance testing when constructing salvage therapy regimens. Clinicians should consult with an expert to interpret the results of resistance assays. **(I)**

Clinicians should use a drug from a class that was not used in the first regimen when constructing a second-line regimen. **(I)**

When treating patients with high levels of HIV drug resistance, clinicians should consider using agents in novel ARV classes or with unique resistance profiles, such as the entry inhibitors or drugs available through clinical trials or expanded access.

Acute HIV Infection

Note: In the medical literature, as in this section, the terms *acute* HIV infection and *primary* HIV infection are interchangeable. For consistency, the term *acute* HIV infection is used in these guidelines.

Diagnosis of Acute HIV Infection

Clinicians should maintain a high level of suspicion for acute HIV infection in all patients presenting with a compatible clinical syndrome (see Table 10 in the original guideline document). When acute retroviral syndrome is suspected, a plasma HIV ribonucleic acid (RNA) assay should be used in conjunction with an HIV-1 antibody test to diagnose acute HIV infection. **(III)**

Confirmatory HIV antibody testing should be performed 3 to 6 weeks after diagnosis by HIV RNA testing. **(III)**

Management of Acute HIV Infection

Clinicians should counsel patients about the increased risk of transmitting HIV during acute HIV infection.

Clinicians should obtain baseline genotypic testing in the setting of acute infection, regardless of whether ARV is being initiated.

Clinicians should consult with an HIV Specialist to weigh the benefits and risks of initiating therapy in patients with acute HIV infection and should refer for research opportunities as appropriate (see Appendix F in the original guideline document). **(III)**

The clinician should counsel the patient regarding potential limitations of HAART during acute infection, and individual decisions should be made only after weighing the risks of therapy against the theoretical benefit of treatment (see Table 11 in the original guideline document). **(III)**

If the clinician and patient have made a decision to use ARV therapy for acute HIV infection, treatment should be based on the results of genotypic testing and implemented with the goal of suppressing plasma HIV RNA levels to below detectable levels. **(I)**

Management of Treatment Interruption

Patients should be discouraged from stopping HAART without first consulting with their clinician. **(III)**

When HAART is interrupted, clinicians should inform patients of the potential increased risk of transmitting HIV. Risk-reduction counseling and prevention interventions should be intensified at this time.

Before interrupting HAART in patients receiving ARV medications with prolonged half-lives, such as NNRTIs, clinicians should consult with an HIV Specialist for guidance on how to avoid the emergence of resistance.

Clinicians should not interrupt lamivudine, emtricitabine, or tenofovir (or combination pills containing these drugs) in patients who are co-infected with chronic hepatitis B without implementing another hepatitis B virus (HBV) treatment option.

Strategic treatment interruption (STI) is not recommended in the management of the HIV-infected patient. **(I)**

Referring Patients to Research Studies

Referral of patients to research protocols should be 1) to provide treatment or diagnostic options that may be otherwise unavailable and that may enhance treatment outcome, and 2) to attempt to answer a relevant research question. **(III)**

Patients should be fully informed of any financial benefit their referral to a research study might have for the referring clinician. **(III)**

Patients should be informed that research studies often require major commitments of time and effort in addition to potential unforeseeable risk. **(III)**

The clinician should provide assistance to patients who want to participate in research studies. **(III)**

Definitions:

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trials
II. Evidence from one or more well-designed clinical trials without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Initiating Antiretroviral Therapy
- Monitoring Antiretroviral Therapy

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Antiretroviral Therapy

- The preservation and/or restoration of immune function
- Improvement of overall health and the prolongation of life
- The suppression of viral replication
- The possible decrease in risk of viral transmission to others (including fetal transmission)

Early Therapy

- Control of viral replication is easier to achieve and maintain
- Delay or prevention of immune system compromise
- Lower risk of resistance with complete viral suppression
- Possible decreased risk of HIV transmission

Delayed Therapy

- Minimization of negative effects on quality of life
- Avoidance of drug-related adverse events
- Delayed development of drug resistance
- Preservation of maximum number of available and future drug options until risk of human immunodeficiency virus (HIV) disease progression is higher

POTENTIAL HARMS

Antiretroviral Therapy

- Adverse effects of the medications on quality of life (for adverse effects and drug interactions of specific antiretroviral drugs, see tables in appendices A and B of the original guideline)
- Known, and as yet unknown, long-term drug toxicities, including potential fetal toxicity
- The development of human immunodeficiency virus (HIV) drug resistance to drugs currently available and possibly to those not yet available, which may limit future treatment options

Early Therapy

- Drug-related reduction in quality of life

- Greater cumulative drug-related adverse events
- Earlier development of drug resistance if viral suppression is suboptimal
- Limitation in future ARV treatment options

Delayed Therapy

- Possible risk of further or irreversible immune system depletion
- Possible greater difficulty in suppressing viral load
- Potential increased risk of HIV transmission

CONTRAINDICATIONS

CONTRAINDICATIONS

- Contraindications to efavirenz include known adverse reactions to efavirenz, first-trimester pregnancy, or strong likelihood of becoming pregnant.
- Clinicians should not use nevirapine as part of the initial regimen in women with CD4 counts >250 cells/mm^3 or men with CD4 counts >400 cells/mm^3 because of an increased incidence of hepatotoxicity.
- Clinicians should not prescribe didanosine for patients who have a history of pancreatitis.
- In the setting of hepatotoxicity related to nevirapine, patients should not be re-challenged with nevirapine.
- See appendices A and B of the original guideline document for contraindicated combinations of antiretroviral drugs and other medications.
- The following therapies and components are contraindicated for initial therapy:
    - Emtricitabine + Lamivudine
    - Fosamprenavir + Lopinavir/ritonavir (co-formulated as Kaletra)
    - Hydroxyurea
    - Ritonavir + Nelfinavir
    - Stavudine + Zidovudine
    - Any monotherapy or two-drug therapy

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with HIV infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers and consumers through mass mailings and numerous AIDS Institute-sponsored

educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative (CEI), the AIDS Educational Training Centers (AETC) and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the New York State Department of Health (NYSDOH) Distribution Center for providers who lack internet access.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the CEI and the AETC. The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2008 Jan. 115 p. [18 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

New York State Department of Health - State/Local Government Agency [U.S.]

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GUIDELINE COMMITTEE

Medical Care Criteria Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2007 Aug. 50 p. [18 references]

GUIDELINE AVAILABILITY

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site.

AVAILABILITY OF COMPANION DOCUMENTS

This guideline is also available as a Personal Digital Assistant (PDA) download from the New York State Department of Health AIDS Institute Web site.

PATIENT RESOURCES

None available

NGC STATUS

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